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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,687	06/13/2006	Pasqua Anna Oreste	GRT/3687-177	2203

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
11/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,687	ORESTE ET AL.	
	Examiner	Art Unit	
	Layla Bland	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-27 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/13/2006, 10/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group II, claims 17-27 and 32-35, in the reply filed on October 9, 2007, is acknowledged. Claims 1-35 are pending in this application. Claims 1-16, 28-31 are withdrawn from consideration as being drawn to a non-elected invention. Claims 17-27 and 32-35 are examined on the merits herein.

Claim Objections

Claim 32 is objected to because of the following informalities: "pharmacological" should be "pharmacologically." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the recitation of claim 1. Note that claim 1 is withdrawn from further consideration. Insertion of the recitation of claim 1 into claim 17 would be favorably considered. In order to expedite prosecution, claim 17 will be examined inserting the recitation of claim 1 into claim 17, as has apparently been intended.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 22 recites the limitation "presenting an unity (a') at the reducing end of the majority of the chains." It is unclear what "an unity (a')" represents.

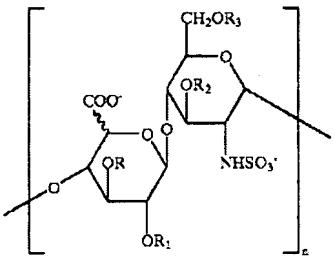
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-21, 23-25, 27, and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Oreste et al. (WO 02/50125, June 27, 2002, PTO-1449 submitted June 13, 2006).

Oreste et al. teach glycosaminoglycans derived from K5 polysaccharides [see abstract] which consist of a mixture of chains in which at least 90% of said chains have the formula



, wherein 40-60% of the uronic acid units are iduronic acid, the sulfation degree is 2.3 to 2.9, R_3 is 85% to 95% SO_3^-, R_2 is 17-21% SO_3^-, R_1 is about 15-35% SO_3^- in iduronic units and 0-5% SO_3^- in glucuronic units, R is from 20-40% SO_3^- in glucuronic units and 0-5% in iduronic units, and the mean molecular weight

is from about 6,000 to about 8,000 [claims 25 and 31]. In one embodiment, n is from 3 to 15 [claim 29]. Oreste et al. also teach pharmaceutical compositions comprising these compounds and pharmaceutically acceptable carriers [claim 38]. The compounds have high antithrombin activity and are useful for the control of coagulation [see abstract].

Oreste et al. are silent on the structure at the reducing end of the majority of the chains. However, the skilled artisan would understand that compounds made by the methods of Oreste et al., wherein the compounds are prepared from a low molecular weight fraction of K5 [page 15, lines 1-4], or fractionated [page 15, lines 21-24], or depolymerized early in the synthesis [page 14, lines 27-31] would necessarily have the claimed sulfated structure at the reducing end of the majority of the chains. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claims 17 and 33-25 are product-by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). The product-by-process claim was rejected

because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.). See MPEP 2113. The limitation "depolymerized" is also interpreted as drawn to the method of production, which results in a low molecular weight product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oreste et al. (WO 02/50125, June 27, 2002, PTO-1449 submitted June 13, 2006) in view of Naggi et al. (Carbohydrate Research 336 (2001) 283-290, PTO-1449 submitted June 13, 2006).

Oreste et al. teach as set forth above.

Oreste et al. do not teach derivatives having a content of 45-55% in glucosamine 3-O-sulfate.

Naggi et al. teach that sulfation at C-3 of central $GlcNSO_3$ residue increases the aXa activity of heparin [page 288, first paragraph]. Naggi et al. also teach desulfation kinetics of sulfated heparin in DMSO-MeOH at different times and temperatures, and

show that derivatives with 45-60% glucosamine 3-O-sulfate can be obtained at 65°C-90°C, for 30-90 minutes [page 286, Table 1].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare compounds similar to those taught by Oreste et al., having 45-55% of glucosamine 3-O-sulfate. The skilled artisan would have been motivated to do so in order to enhance the activity of the compounds taught by Oreste et al. Naggi et al. teach that sulfation at C-3 of the central $GlcNSO_3$ residue increases the aXa activity of heparin and teach conditions for selective desulfation of supersulfated low-molecular weight heparin. The compounds of Oreste et al. are structurally similar to heparin and function similarly, so the skilled artisan could extend the teachings of Naggi et al. to the teachings of Oreste et al. with a reasonable expectation of success.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-27 and 32-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37-59 of copending Application No. 11/440,749. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in each application are drawn to substantially overlapping genera of compounds and pharmaceutical compositions comprising such. The claims of copending Application No. 11/440,749 do not require a specific structure at the reducing end of the majority of the chains, but this is an inherent feature of the compounds due to the method of their production.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17-27 and 32-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 14-36 of copending Application No. 11/030,156. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in each application are drawn to substantially overlapping genera of compounds and pharmaceutical compositions comprising such. The claims of copending Application No. 11/030,156 do not require a specific structure at the reducing end of the majority of the chains, but this is an inherent feature of the compounds due to the method of their production.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17-27 and 32-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-25 of copending Application No. 10/868,359. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in each application are drawn to substantially overlapping genera of compounds and pharmaceutical compositions comprising such.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17-27 and 32-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 35-62 of copending Application No. 09/950,003. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in each application are drawn to substantially overlapping genera of compounds and pharmaceutical compositions comprising such. The claims of copending Application No. 09/950,003 do not require a specific structure at the reducing end of the majority of the chains, but this is an inherent feature of the compounds due to the method of their production.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (571) 272-9572. The examiner can normally be reached on M-R 8:00AM-5:00PM UST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1623
October 29, 2007

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11/07/07
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